

## AMENDMENTS TO THE CLAIMS:

Please amend claims 1, 3, 4, 5, 12-14, 17, 18, 19, 21, 64, 67, 68-74, 76 and 79 as follows:

1. (Currently amended) A method for identifying a compound that modulates a ~~heat shock protein- ( an HSP ) - alpha-(2)-macroglobulin-(  $\alpha$ 2M )~~ receptor-mediated process, comprising:

- (a) contacting a test compound with: (i) an isolated ~~alpha-(2)-macroglobulin  $\alpha$ 2M~~ receptor, or a ligand-binding fragment thereof; and (ii) a purified heat shock protein, or a binding fragment thereof, or a purified HSP-peptide complex; and
- (b) measuring the level of ~~alpha-(2)-macroglobulin-receptor activity or expression~~ HSP binding activity, HSP uptake activity, or HSP-mediated antigen representation activity,

such that if the level of ~~activity or expression~~ HSP binding activity, HSP uptake activity, or HSP-mediated antigen representation activity measured in (b) differs from the level of ~~alpha-(2)-macroglobulin-receptor activity~~ HSP binding activity, HSP uptake activity, or HSP-mediated antigen representation activity in the absence of the test compound, then a compound that modulates an HSP- $\alpha$ 2M receptor-mediated process is identified.

2. (Previously amended) The method of claim 1, in which the compound identified is an antagonist which interferes with an HSP- $\alpha$ 2M receptor-mediated process.

3. (Currently amended) The method of claim 1, in which the test compound is an antibody specific for the ~~alpha-(2)-macroglobulin  $\alpha$ 2M~~ receptor.

4. (Currently amended) The method of claim 1, in which the test compound is an antibody is specific for alpha (2) macroglobulin.

5. (Currently amended) The method of claim 1, in which the test compound is an antibody is specific for a heat shock protein.

6. (Original) The method of claim 1, in which the test compound is a small molecule.
7. (Original) The method of claim 1, in which the test compound is a peptide.
8. (Original) The method of claim 7, in which the peptide comprises at least 5 consecutive amino acids of the alpha (2) macroglobulin receptor (SEQ ID NO.: 7).
9. (Original) The method of claim 7, in which the peptide comprises at least 5 consecutive amino acids of alpha (2) macroglobulin (SEQ ID NO.: 4).
10. (Original) The method of claim 7, in which the peptide comprises at least 5 consecutive amino acids of a heat shock protein sequence.
11. (Previously amended) The method of claim 1, in which the compound is an agonist which enhances an HSP- $\alpha$ 2M receptor-mediated process.
12. (Currently amended) The method of claim 1 in which the HSP- $\alpha$ 2M receptor-mediated process affects diabetes or other ~~an~~ autoimmune disorder, a disease or disorder involving disruption of antigen presentation or endocytosis, a disease or disorder involving cytokine clearance or inflammation, a proliferative disorder, a viral disorder or other infectious disease, hypercholesterolemia, Alzheimer's disease, ~~diabetes~~, or osteoporosis.
13. (Currently amended) A method for identifying a compound that modulates an HSP- $\alpha$ 2M receptor-mediated process, comprising:
- (a) contacting a test compound with (i) a cell expressing an alpha (2) macroglobulin  $\alpha$ 2M receptor or ligand-binding fragment thereof ~~expressing cell~~ and (ii) a purified heat shock protein, or fragment thereof, or a purified HSP-peptide complex; and
  - (b) measuring the level of alpha (2) macroglobulin receptor ~~HSP~~ binding activity, HSP uptake activity, or HSP-mediated antigen representation activity in the cell,
- such that if the level of alpha (2) macroglobulin receptor ~~HSP~~ binding activity, HSP uptake activity, or HSP-mediated antigen representation activity measured in (b) differs from

the level of ~~alpha (2) macroglobulin receptor~~ HSP binding activity, HSP uptake activity, or HSP-mediated antigen representation activity in the absence of the test compound, then a compound that modulates an HSP- $\alpha$ 2M receptor-mediated process is identified.

14. (Currently amended) The method of claim 1 or 13 wherein the ~~alpha (2) macroglobulin receptor activity~~ HSP binding activity is measured is ~~the ability to bind to a heat shock protein.~~

15 - 16. (Cancelled)

17. (Currently amended) The method of claim 1 or 13 ~~wherein the alpha (2) macroglobulin receptor activity measured is the ability to bind to a heat shock protein,~~ wherein measuring the level of ~~alpha (2) macroglobulin receptor activity~~ HSP binding activity of step (b) comprises measuring the amount of heat shock protein, or binding fragment thereof, bound to the ~~alpha (2) macroglobulin~~  $\alpha$ 2M receptor, or ligand-binding fragment thereof, such that if the amount of bound heat shock protein measured in (b) differs from the amount of bound heat shock protein measured in the absence of the test compound, then a compound that modulates the binding of an HSP to the  $\alpha$ 2M receptor is identified.

18. (Currently amended) The method of claim 1 or 14, in which the ~~alpha (2) macroglobulin~~  $\alpha$ 2M receptor or ligand-binding fragment thereof contacted in step (a) is on a cell surface.

19. (Currently amended) The method of claim 1 or 14, wherein the ~~alpha (2) macroglobulin~~  $\alpha$ 2M receptor or ligand-binding fragment thereof is immobilized to a solid surface.

20. (Original) The method of claim 19 wherein the solid surface is a microtiter dish.

21. (Currently amended) The method of claim 14 wherein the ~~amount of bound heat shock protein~~ HSP binding activity is measured by contacting the cell with a heat shock protein-specific antibody.

22. (Previously amended) The method of claim 14 wherein the heat shock protein is labeled and the amount of bound heat shock protein is measured by detecting the label.

23. (Original) The method of claim 22 wherein the heat shock protein is labeled with a fluorescent label.

23-63. (Cancelled)

64. (Currently amended) The method of claim 1 or 13, wherein the ~~alpha (2) macroglobulin~~ α2M receptor or ligand-binding fragment thereof is purified.

65-66. (Cancelled)

67. (Currently amended) The method of claim 14, wherein the ~~derivative, analog, α2M receptor or ligand-binding fragment thereof, or domain of the alpha (2) macroglobulin receptor~~ α2M receptor or ligand-binding fragment thereof is purified.

68. (Currently amended) A method for identifying a compound that modulates an HSP-α2M receptor-mediated process, comprising:

- (a) contacting a test compound with ~~an alpha (2) macroglobulin receptor-expressing cell~~ (i) a cell expressing an α2M or ligand-binding fragment thereof and (ii) a purified heat shock protein, or fragment thereof, or a purified HSP-peptide complex; and
- (b) measuring the level of ~~alpha (2) macroglobulin~~ α2M receptor activity by a signal transduction activity assay, heat shock protein uptake assay, chemotaxis assay, or calcium ion concentration assays,

such that if the level of ~~alpha (2) macroglobulin~~ α2M receptor activity measured in (b) differs from the level of ~~alpha (2) macroglobulin~~ α2M receptor activity in the absence of the test compound, then a compound that modulates an HSP-α2M receptor-mediated process is identified.

69. (Currently amended) A method for screening a plurality of molecules for one or more molecules having the ability to modulate, directly or indirectly, the antigen presentation activity of ~~alpha (2) macroglobulin~~ α2M receptor-expressing cells, comprising:

- (a) contacting said plurality of molecules with ~~said the alpha-(2)-macroglobulin~~ α2M receptor-expressing cells and a purified complex of a heat shock protein and the antigenic peptide;
- (b) measuring antigen presentation by said ~~alpha-(2)-macroglobulin~~ α2M receptor-expressing cells in the presence of said plurality of molecules; and
- (c) comparing antigen presentation activity by said ~~alpha-(2)-macroglobulin~~ α2M receptor-expressing cells in the presence of said plurality of molecules with antigen presentation activity by said ~~alpha-(2)-macroglobulin~~ α2M receptor-expressing cells in the absence of said plurality of molecules

wherein a lower or higher degree of antigen presentation indicates that one or more molecule(s) modulates the antigen presentation activity by said ~~alpha-(2)-macroglobulin~~ α2M receptor-expressing cells.

70. (Currently amended) A method for screening an antibody specific to a heat shock protein or an ~~alpha-(2)-macroglobulin~~ α2M receptor for the ability to modulate, directly or indirectly, the antigen presentation activity ~~alpha-(2)-macroglobulin~~ α2M receptor-expressing cells, comprising:

- (a) contacting the antibody with the ~~alpha-(2)-macroglobulin~~ α2M receptor-expressing cells and a purified complex of a heat shock protein and the antigenic peptide;
- (b) measuring antigen presentation by the ~~alpha-(2)-macroglobulin~~ α2M receptor-expressing cells in the presence of the antibody; and
- (c) comparing antigen presentation activity by said ~~alpha-(2)-macroglobulin~~ α2M receptor-expressing cells in the presence of the antibody with antigen presentation activity by the ~~alpha-(2)-macroglobulin~~ α2M receptor-expressing cells in the absence of the antibody,

wherein a lower or higher degree of antigen presentation indicates that the antibody modulates the antigen presentation activity by said ~~alpha-(2)-macroglobulin~~ α2M receptor-expressing cells.

71. (Currently amended) A method for screening a molecule for the ability to modulate, directly or indirectly, the antigen presentation activity of ~~alpha-(2)-macroglobulin~~ α2M receptor-expressing cells, comprising:

- (a) contacting the molecule with purified ~~alpha (2) macroglobulin~~ α2M receptor-expressing cells and a purified complex of a heat shock protein and an antigenic peptide;
- (b) measuring antigen presentation by the ~~alpha (2) macroglobulin~~ α2M receptor-expressing cells in the presence of the molecule; and
- (c) comparing antigen presentation activity by the ~~alpha (2) macroglobulin~~ α2M -expressing cells in the presence of the molecule with antigen presentation activity by the ~~alpha (2) macroglobulin~~ α2M receptor-expressing cells in the absence of the molecule,

wherein a lower or higher degree of antigen presentation indicates that the molecule modulates the antigen presentation activity by said ~~alpha (2) macroglobulin~~ α2M receptor-expressing cells.

72. (Currently amended) A method for screening a plurality of molecules for one or more molecules having the ability to modulate, directly or indirectly, the ability of an ~~alpha (2) macroglobulin~~ α2M receptor-expressing cell to ~~stimulate the activation of~~ activate cytotoxic T cells *in vitro* comprising:

- (a) contacting said plurality of molecules with: (i) cells expressing ~~alpha (2) macroglobulin~~ α2M receptor; (ii) a purified complex of a heat shock protein and a peptide; and (iii) cytotoxic T cells, under conditions conducive to the activation of cytotoxic T cells;
- (b) comparing the activation in vitro of said T cells with the activation in vitro of T cells in the absence of said plurality of molecules,

wherein a lower or higher degree of T cell activation indicates that one or more molecules in said plurality of molecules modulates the ability of the ~~alpha (2) macroglobulin~~ α2M receptor -expressing cells to ~~stimulate the activation of~~ activate cytotoxic T cells against the peptide.

73. (Currently amended) A method for screening an antibody specific to a heat shock protein or an ~~alpha (2) macroglobulin~~ α2M receptor for the ability to modulate, directly or indirectly, the ability of an ~~alpha (2) macroglobulin~~ α2M receptor-expressing cell to ~~stimulate the activation of~~ activate cytotoxic T cells *in vitro* comprising:

- (a) contacting the antibody with: (i) cells expressing ~~alpha (2) macroglobulin~~ α2M receptor; (ii) a purified complex of a heat shock protein and a peptide; and (iii)

cytotoxic T cells, under conditions conducive to the activation of cytotoxic T cells;

- (b) comparing the activation in vitro of said T cells with the activation in vitro of T cells in the absence of said plurality of molecules,

wherein a lower or higher degree of T cell activation indicates that the antibody modulates the ability of the ~~alpha (2) macroglobulin~~ α2M receptor-expressing cells to ~~stimulate the activation of~~ activate cytotoxic T cells against the peptide.

74. (Currently amended) A method for screening a molecule for the ability to modulate, directly or indirectly, the ability of an ~~alpha (2) macroglobulin~~ α2M receptor-expressing cell to ~~stimulate the activation of~~ activate cytotoxic T cells *in vitro* comprising:

- (a) contacting said molecule with: (i) purified cells expressing alpha ~~alpha (2) macroglobulin~~ α2M receptor; (ii) a purified complex of a heat shock protein and a peptide; and (iii) cytotoxic T cells, under conditions conducive to the activation of cytotoxic T cells;
- (b) comparing the activation in vitro of said T cells with the activation in vitro of T cells in the absence of said plurality of molecules,

wherein a lower or higher degree of activation indicates that one or more molecules in said plurality of molecules modulates the ability of the alpha (2) macroglobulin -expressing cells to ~~stimulate the activation of~~ activate cytotoxic T cells against the peptide.

75. (Previously added) The method of any one of claims 70, 71, or 72, wherein the activity is measured by a cytokine release assay.

76. (Currently amended) The method of any one of claims 13, ~~69, 70, 71, 72, 73, or 74~~, wherein the ~~alpha (2) macroglobulin~~ α2M receptor or ligand-binding fragment thereof is recombinantly expressed in the cell.

77. (Previously added) The method of claim 1 or 13 wherein HSP uptake activity is measured.

78. (Previously added) The method of claim 1 or 13 wherein HSP -mediated antigen representation activity is measured.

79. (Currently amended) The method of any one of claims 69, 70, 71, 72, 73, or 74, wherein the ~~alpha (2) macroglobulin~~  $\alpha$ 2M receptor is recombinantly expressed in the cell.